Sacral Neuromodulation for Anorectal Dysfunction

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Background of Sacral Neuromodulation for Anorectal Dysfunction

The concept of recruiting residual function of the anorectal continence organ by stimulation of its peripheral nerve supply, the sacral spinal nerves, was introduced in 1994 [1].

Observation in patients treated for urinary dysfunction with sacral nerve stimulation revealed a potentially therapeutic effect on anorectal continence function. Ever since, the understanding of underlying mode of action has increased. Initially, the idea was an efferent nerve stimulating effect: today, it is appreciated that the effect of sacral spinal nerve stimulation (SNS)/sacral neuromodulation (SNM) is not confined to efferent nerves but also affects afferent nerve fibers, and it is not limited to the peripheral nerve system. As the mode of action is manyfold, there are no distinct physiological and morphological criteria, which allow to predict the therapeutic potential of the therapy in an individual patient. Based on this concept and the advantage of a testing phase to evaluate the therapeutic potential of SNM, the spectrum of application broadened over the years, even beyond the field of incontinence [2].

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SNM Technique

Patient selection is based on the outcome of a test stimulation phase: no clinical or physiologic predictor of success of chronic stimulation exists, and thus decision-making for implantation of a permanent device is based solely on the outcome of temporary test stimulation, usually of 2 weeks duration. Prerequisites for the test stimulation are residual sphincter function, an existing neuromuscular connection to the sphincter (tested by observation of voluntary squeeze or reflex activity after pinprick), and accessibility of the target sacral spinal nerves S3 and S4. Thus, the spectrum of application is not limited to specific physiological or morphological conditions.

The stimulation system consists of a fully implantable electrode placed close to a target nerve at the level of the sacral spinal nerves, most commonly S3 or S4, connected to an impulse generator placed in a subcutaneous pocket, which can be programmed and activated via telemetry.

The operative technique and the process of patient selection for permanent therapeutic SNM are standardized. With so-called percutaneous nerve evaluation (PNE), the sacral spinal nerves S3 and S4 are stimulated with needle electrodes placed through the dorsal sacral foramen. This aims to determine the single sacral spinal nerve functionally relevant to the innervation of the striated pelvic floor and anal sphincter muscles and to demonstrate whether nerve stimulation can induce muscular contraction.

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If PNE is successful, it is followed by the placement of one or more electrodes in the proximity of one or more target spinal nerves. Two techniques are available: temporary electrodes or electrodes that can remain in place for chronic stimulation if this phase is successful. The latter are quadripolar, so-called "tined lead" electrodes, and are placed with fluoroscopy guidance [3]. Both types of electrodes are connected to an external pulse generator for this test stimulation period.

If tined leads have been used and results indicate clinical efficacy, a pulse generator (IPG) is placed, usually in a subcutaneous pocket in the gluteal area. If temporary electrodes have been used, the complete neurostimulation system – electrode and pulse generator – needs to be implanted. Stimulation usually starts early after the implantation of the IPG, which is programmed by telemetry. The chronic stimulation pattern is standardized: 15 Hz, 210 μsec, and continuous or on/off cycle 5 sec/1 sec; voltage is adapted to the patients' perception of the stimulation in the anal and perineal region. The IPG can be deactivated and the intensity of stimulation changed within a preset range by the patient with a handheld device, the so-called patient programmer. During the PNE phase, bowel habits are documented with standardized bowel diaries (which are also used for follow-up) and then compared with pretest function. Commonly, a 50% improvement in symptoms – episodes of incontinence or days with incontinence episodes – is considered an indication for permanent stimulation.

Indication

Fecal Incontinence

For fecal incontinence (FI), commonly, a 50% improvement in symptoms with incontinence episodes is considered an indication for permanent stimulation. The predictive value of a positive test result is high: in approximately 80% of patients, the outcome of the test stimulation is at least equaled with permanent stimulation [2, 4]. The relevance of a false-negative test stimulation is unknown.

With the help of the highly predictive test stimulation, the spectrum of indications has been continuously expanded. Initially, the technique was confined to patients presenting with a weak, but morphologically intact, striated muscle pelvic floor and anal sphincter. Today, SNM is successfully applied to a wide etiologic spectrum [2, 3] such as weak external anal sphincter (with or without a deficit or defect of the smooth muscle internal anal sphincter), structuraö defects of the external anal sphincter of up to 180° [5]; fecal incontinence with or without urinary incontinence, low anterior resection syndrome [6] and neurogenic FI [7].

In recent years, the outcome has been increasingly presented on the basis of an intention-to-treat analysis (ITT). With this approach, clinically test stimulations are considered part of the treatment – not part of the diagnostic workup – and are consequently counted as failures if negative. Failure of the test stimulation, also dependent on patient selection, can reach up to 27% [2].

Constipation

As for incontinence, a symptom alleviation of 50% in constipation is commonly accepted to indicated chronic stimulation with a fully implantable neurostimulation system. Data of SNM for constipation are less robust than for incontinence treatment. Many series report a symptom improvement, which is less than in FI; however, outcome has been questioned recently [8]. A recent single report describes symptom improvement in a distinct group of patients presenting with constipation because of rectal hyposensitivity during test stimulation [9].

Contraindications

Contraindications to SNM are pathological conditions of the sacrum preventing adequate electrode placement, skin disease at the area of implantation, severe anal sphincter damage, trauma sequelae with micturition disorders or low bladder capacity, pregnancy, bleeding risk, psycho-

logical instability, low mental capacity, the presence of a cardiac pacemaker (although compatibility can be assessed) or implantable defibrillator, and the need for MRI (except head coil).

Morbidity of SNM is low, and severe complications are rare: device removal occurs in around 3%, and the overall complication rate ranges around 15% in patients with permanent implants [10, 11]. In a collective of 120 patients studied under a strict protocol, the cumulative revision rate at 5 years was 24%; after 5 years, the system was still in use in 81% [12].

The therapy requires maintenance: the IPG needs to be exchanged once the battery is depleted, and a substantial proportion of patients require repeated adjustment of the stimulation parameters. Indeed, a study revealed that 47% of the follow-up budget was used for 27% of the patients – those patients with suboptimal outcome [13].

Results

Fecal Incontinence

Usually, outcome is reported describing frequencies of incontinence episodes and/or applying incontinence scores such as the Cleveland Clinic Florida Fecal Incontinence Score (CCF-FIS) and quality of life scores. The reproducibility of this technique's clinical efficacy has been demonstrated in multiple studies: with chronic SNM, the frequency of incontinence episodes is reduced (Tables 37.1, 37.2, and 37.3), the CCF-FIS is reduced (Table 37.2), the ability to postpone bowel emptying is increased, and the quality of life is improved [10]. Long-term follow-up shows sustained efficacy: a median of 36% (4–52) of patients with chronic SNM experiences 100% symptom improvement, and 76% (21–96), a 50% improvement [2] if per-protocol analysis is applied (evaluating only those patients with a permanent device implanted based on the positive outcome of a test phase). Overall outcome has been seen to be poorer in patients with an underlying high-grade internal rectal intussusception [14], but no other correlation with morphological and physiological conditions or demographic features has been convincingly demonstrated [2].

In recent years, the outcome has been increasingly presented on the basis of an intention-to-treat analysis (ITT). With this approach, clinically unsuccessful test stimulations are considered part of the treatment – not part of the diagnostic workup – and are consequently counted as failures (Table 37.1). Failure of the test stimulation, also dependent on patient selection, can reach up to 27% [2].

Table 37.1 Chronic sacral nerve neuromodulation (SNM) for fecal incontinence (FI): >50% improvement of incontinence episodes/week, studies with at least 50 patients

Author	Year	Patients (n) (baseline)	Patients (n) (follow-up)	Median follow-up (month)	>50% improvement incontinence episodes/week	Intention-to-treat: 50% improvement incontinence episodes/week
Melenhorst et al.	2007	100	100	26[b]	79	59
Dudding et al.	2008	51	48	24	65	52
Tjandra et al.	2008	53	53	12[a]	71	63
Govaert et al.	2009	173	169	35[b]	77	53
Hollingshead et al.	2011	86	18	60[a]	83	n.a.
Uludag et al.	2011	50	50	85	84	n.a.
Duelund-Jakobsen et al.	2012	158	91	46	75	n.a.
Hull et al.	2013	120	76	60[a]	89	53
Altomare et al.	2015	272	228	84	78	50

Modified after Thin et al. [17]. [a]values at specific time point; [b]mean; n.a. not available

Table 37.2 Chronic sacral neuromodulation (SNM) for fecal incontinence (FI): Cleveland Clinic Incontinence Score, studies with at least 50 patients

Author	Year	Patients (n) (baseline)	Patients (n) (follow-up)	Median follow-up (months)	Median score baseline (range)	Median score follow-up (range)	*p*-value
Tjandra et al.	2008	53	53	12[a]	16 (1)[b]	1 (2)[b]	<0.001
Altomare et al.	2009	60	52	74[b]	15 (4)[b]	5 (5)[b]	<0.001
Brouwer et al.	2010	55	13	48[a]	15 (13–18)	6 (2–8)	0.008
Faucheron et al.	2010	87	87	45	13 (6–19)[b]	8 (1–17)[b]	n.a.
Michelsen et al.	2010	126	10	72[a]	20 (12–20)	7 (2–11)	<0.001
Gallas et al.	2011	200	54	24[a]	14 (2–20)	7 (0–19)	0.001
Lim et al.	2011	53	41	51[b]	12 (9–15)	8 (5–11)	0.001
Wong et al.	2011	61	61	31	14 (n.a.)	8 (n.a.)	n.a.
Faucheron et al.	2012	57	42	63	14 (4–19)	7 (1–16)	<0.001
Damon et al.	2013	102	101	48[b]	14 (3)	9 (1)	<0.0001
Maeda et al.	2014	108	101	60[a]	16 (6–20)	8 (0–19)	<0.0001
Altomare et al.	2015	272	228	84	16 (13–18)	7 (4–12)	<0.001
Duelund-Jakobsen et al.	2016	164	n.a.	22	15 (3–20)	9 (0–20)	<0.001

Modified after Thin et al. [17]. [a]values at specific time point; [b]mean; n.a. not available

Table 37.3 Chronic sacral neuromodulation (SNM) for fecal incontinence (FI): incontinence episodes, studies with at least 50 patients

Author	Year	Patients (n) PNE	Patients (n) (implants)	Patients (n) (follow-up)	Median follow-up (months)	Incontinence episodes/ week median (range)		*P* value
						Baseline	Last follow-up	
Uludag et al.	2004	63	50 (79%)	6	24[a]	8 (n.a.)	1 (n.a.)	n.s.
Melenhorst et al.	2007	134	100 (75%)	6	60[a]	10 (n.a.)[b]	2 (n.a.)[b]	<0.001
Dudding et al.	2008	60	51 (85%)	48	24	6 (0–81)	1 (0–59)	n.a.
Tjandra et al.	2008	60	53 (88%)	53	12[a]	10 (13)[b]	3 (10)[b]	<0.001
Altomare et al.	2009	94	60 (64%)	52	74[b]	4 (n.a.)[b]	1 (n.a.)[b]	0.004
Michelsen et al.	2010	167	126 (74%)	49	12[a]	8 (n.a.)	1 (n.a.)	<0.001
Hollingshead et al.	2011	113	86(76%)	86	33	9 (7)[b]	1 (2) [b]	<0.001
Uludag et al.	2011	n.a.	50	n.a.	60	8 (n.a.)	0 (n.a.)	<0.002
Duelund-Jakobsen et al.	2012	n.a.	147	147	46	6 (n.a.)	1 (n.a.)	<0.001
Hull et al.	2013	133	120 (90%)	76	>60	9 (n.a.)	2 (n.a.)	<0.0001
Altomare et al.	2015	407	272 (67%)	228	84	7 (4–11)	0.3 (0–3)	<0.001
Janssen et al.	2017	374	325 (87%)	?	7.1 years	5 (n.a.)[b]	1(n.a.)[b]	<0.001

Modified after Thin et al. [17]. [a]values at specific time point; [b]mean; n.a. not available

Constipation

Like in incontinence, the efficacy of SNN in the treatment of constipation is monitored by using symptom and quality of life scores. Existing studies include patients with heterogeneous causes of constipation. This prevents firm conclusions. In most studies, a symptom improvement is noted. Outcome is poorer when compared to SNM for FI (Table 37.4). While failure rate is higher, the general risk of complications is not different from other indications for SNM.

Table 37.4 Sacral neuromodulation (SNM) for constipation

Author	Year	Patients (*n*)	Follow-up	*n* Temporary	*n* Permanent	Improvement (intention-to-treat: %)
Kenefick et al.	2002	4	8 months (1–11)	ns	4	3/ns
Kenefick et al.	2002	2	12 months	2	2	2/2
Holzer et al.	2008	19	11 months (2–20)	19	8	8/19 (42%)
Vitton et al.	2009	6	2–50 weeks	6	5	0/6 (0%)
Kamm et al.	2010	62	28 months (1–55)	62	45	39/62 (63%)
Maeda et al.	2010	70	28 months (0–70)	70	38	35/38 (54%)
Naldini et al.	2010	15	42 months (24–60)	15	9	6/9
Carriero et al.	2010	13	22 months (12–26)	13	11	6/11
Sharma et al.	2011	21	38 months (18–62)	21	11	10/21 (48%)
Govaert et al.	2012	117	37 months (4–92)	117	68	61/117 (52%)
Knowles et al.	2012	13	19 months	13	11	9/13 (69%)
Ortiz et al.	2012	48	26 months (6–96)	48	23	14/48 (29%)
Graf et al.	2015	44	24 months (4–81)	44	15	5/44 (11%)
Ratto et al.	2015	61	51 months (±15)	61	42	20/61 (33%)
Patton et al.	2016	53	24 months	Ns	53	3/53 (ns)
Zerbib et al.	2017	36	12 months	36	20	11/36 (31%)
Maeda et al.	2017	62	60 months	62	45	14/62 (23%)

Mechanism of Action

The mechanism of action is complex and multifactorial: the effect of SNM is not limited to the anorectal continence organ and the large bowel, affecting the somatomotor, somatosensory, and autonomic nervous systems; it also appears to affect the central nervous system controlling bowel and sphincter activity [15].

Role in the Current Treatment Algorithm

SNM is a surgical therapy. Surgery for FI should only be considered if conservative means do not result in adequate symptom relief. The role of SNM in the evidence-based surgical treatment algorithm of FI is central (Fig. 37.1) [16]. SNM may be used as a singular treatment modality, but it also can be considered as part of a therapy making use of multiple treatments option, e.g., SNM after functional insufficient sphincter repair. The role of SNM in the treatment algorithm is not static. Recent developments like injectable, posterior tibial nerve stimulation, and Gatekeeper/Sphinkeeper challenge its role. The conceptual advantages of SNM are test stimulation, limited invasiveness, reversibility, high patient adherence to therapy, and sustainable long-term results.

In the context of surgical options for constipation, the role of SNM is less defined. Even though it is controversial, it may offer an alternative to much more invasive, resective surgical interventions in an individual patient. When compared with other, mostly resective treatment modalities, it is expected that the advantage of being not very invasive and of being reversible will determine the role of SNM in the therapeutic algorithm of constipation, despite the fact that the outcome is only moderate.

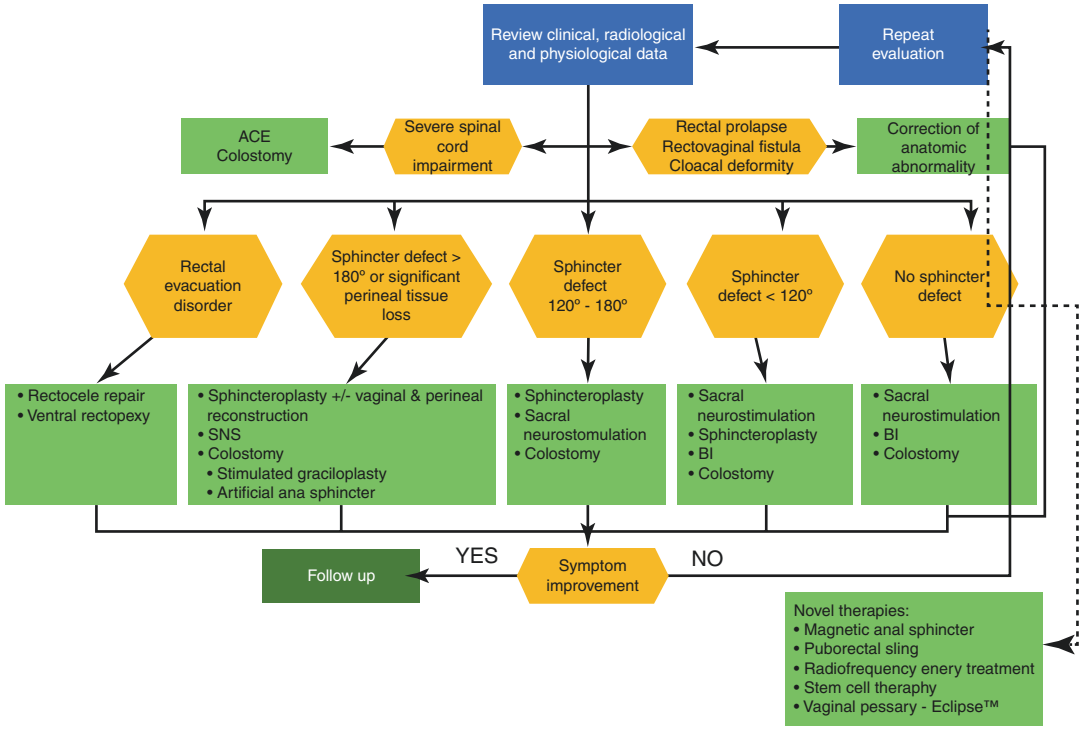

Fig. 37.1 International consultation on fecal incontinence [16]

Summary

SNM for FI should only be considered if conservative means do not result in adequate symptom relief. SNM may be used as a singular treatment modality, but it also can be considered as part of a therapy making use of multiple treatments options. Conceptual advantages of SNM are test stimulation, limited invasiveness, reversibility, high patient adherence to therapy, and sustainable long-term results. In the context of surgical options for constipation, the role of SNM is less defined. Although it is controversial, it may offer an alternative to much more invasive, resective surgical interventions in an individual patient, when compared with other, mostly resective treatment modalities.

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